The following **Listing of the Claims** will replace all prior versions and all prior listings of the claims in the present application:

Listing of the Claims:

1. (Previously presented) A method for preparing a cell line exhibiting directed constitutive hypermutation of a target nucleic acid region, comprising screening a cell population for ongoing target sequence diversification, wherein said screening comprises determining the mutation rate of the target nucleic acid region relative to the mutation rate of a non-target nucleic acid region, and selecting a cell in which the rate of target nucleic acid mutation exceeds that of non-target nucleic acid region by a factor of 100 or more, wherein the rate of mutation in the cell is modulated by genetic manipulation of one or more DNA repair genes, and wherein said genetic manipulation is selected from the group consisting of gene deletion, conversion, and insertion.

2. (Original) A method according to claim 1, wherein the cell line is a lymphoid cell line.

3. (Previously presented) A method according to claim 2, wherein the cell line is an immunoglobulin-expressing cell.

4. (Original) A method according to claim 1, wherein the cell line expresses the target nucleic acid region in a manner that facilitates selection of cells comprising mutants of said region.

5. (Previously presented) A method according to claim 4, wherein the cell line expresses a gene product encoded by the target nucleic acid region on the cell surface.

6. (Previously presented) A method according to claim 1, wherein the cell line comprises a cell type which hypermutates *in vivo*.

7. (Original) A method according to claim 6, wherein the cell line is a Burkitt lymphoma, follicular lymphoma or diffuse large cell lymphoma cell line.

8. (Original) A method according to claim 1, further comprising the steps of isolating one or more cells which display target sequence diversification, and comparing the rate of accumulation of mutations in the target sequences with that in non-target sequences in the isolated cells.

9. (Original) A method according to claim 8, wherein the target sequence is an immunoglobulin V-gene sequence.

10. (Previously presented) A method according to claim 9, wherein cells of said cell population are screened by assessing loss of an expressed immunoglobulin.

11. (Previously presented) A method according to claim 1 or 8, wherein cells of said cell population are screened by assessment of mutation rates by direct sequencing of the target sequences.

12. (Previously presented) A method according to claim 1 or 8, wherein cells of said cell population are screened by an immunofluorescence technique.

13. (Cancelled)

14. (Cancelled)

15. (Previously presented) A method according to claim 1, wherein said one or more genes are Rad51 analogues and/or paralogues.

16. (Previously presented) A method according to claim 1, wherein the genes are selected from the group consisting of Rad51b, Rad51c and analogues and/or paralogues thereof.

17. (Withdrawn) A method for preparing a gene product having a desired activity, comprising the steps of: a) expressing a nucleic acid encoding the gene product in a population of cells according to claim 1, operably linked to a sequence which directs hypermutation; b) identifying a cell or cells within the population of cells which expresses a mutated gene product having the

desired activity; and c) establishing one or more clonal populations of cells from the cell or cells identified in step (b), and selecting from said clonal populations a cell or cells which expresses a gene product having an improved desired activity.

18. (Withdrawn) A method according to claim 17, wherein the cell or cells direct constitutive hypermutation to an endogenous V gene locus.

19. (Withdrawn) A method according to claim 17 or claim 18, wherein the control sequences which direct hypermutation are selected from sequences occurring downstream of a J gene cluster.

20. (Withdrawn) A method according to claim 19, wherein the control sequences comprise elements Ei/MAR, Cκ. plus flanking regions and E3' as defined according to Klix et al., (1998) Eur J. Immunol. 28:317-326.

21. (Withdrawn) A method according to claim 17, wherein the nucleic acid region operatively linked to control sequences which direct hypermutation is an exogenous sequence inserted into the cell or cells.

22. (Withdrawn) A method according to claim 21, wherein the exogenous sequence comprises a heterologous coding sequence operably linked to control sequences homologous to the cell or cells which direct hypermutation.

23. (Withdrawn) A method according to claim 22, wherein an endogenous V region coding sequence is replaced by a heterologous coding sequence.

24. (Withdrawn) A method according to claim 17, wherein the gene product is an immunoglobulin.

25. (Withdrawn) A method according to claim 17, wherein the gene product is a DNA binding protein.

26. (Withdrawn) A method according to claim 17, wherein the desired activity is a binding activity.

27. (Withdrawn) A method according to claim 17, wherein the gene product is an enzyme.

28. (Withdrawn) A method according to claim 17, wherein steps b) and c) are iteratively repeated.

29. (Withdrawn) A cell capable of directed constitutive hypermutation, wherein said cell is a genetically manipulated chicken bursal lymphoma cell line.

30. (Withdrawn) A cell capable of directed constitutive hypermutation, wherein said cell is a genetically manipulated chicken DT40 cell.

31. (Withdrawn) A cell according to claim 30, selected from the group consisting of Δ xrcc2 DT40 and Δ xrcc3 DT40.